

b.) Remarks

Claim 1 has been amended in order to recite the present invention with the specificity required by statute. Claims 43-46, 47 and 48 are cancelled in order to reduce the issues. Additionally, claim 38 is amended for better idiomatic usage and new claim 51 is presented in order to more specifically recite a preferred embodiment of the present invention. For the Examiner's convenience, the subject matter of the amendment may be found in the specification as filed at page 6, line 5 as well as claims 45 and 46. Accordingly, no new matter has been added.

Claims 1-3, 38, 39 and 41-50 are rejected under 35 U.S.C. §103(a) as being obvious over Takayuki (JP 09-285298), Hama (WO 97/40376) and Miyauchi (U.S. Patent No. 5,736,406) in view of Miki (U.S. Patent No. 6,162,607), all of record, for the reasons of record.

In support of the rejection, the Examiner (again) states Takayuki

teach a method of measuring HDL-cholesterol in a specimen such as serum or plasma by treating the specimen with a cholesterol esterase and cholesterol oxidase in the presence of albumin separately derived from the specimen. Takayuki et al teach that the specimen is treated with a polyanion such as a sulfated polysaccharide, particularly dextran sulfate, as well as with a nonionic surfactant.

Hama is said to

teach that having a nonionic surfactant, albumin and bile acid or its salt at a particular concentration is necessary for reaction to occur with HDL cholesterol specifically.

Takayuki and Hama do not expressly teach a method wherein the nonionic surfactant is polyoxyethylene alkylamine, polyoxyethylene alkenylamine, or

polyoxyethylene polycyclic phenyl ether sulfate.

However, according to the Examiner, Miyauchi specifically teaches

the protein solubilizing agent for determining the amount of HDL cholesterol in the sample, cationic, anionic and nonionic surfactants and a bile acid salt are especially preferable among the surfactants such as compounds (VI), (VII) and (VIII) and the bile acid. Examples of the cationic surfactant include oxyethylene dodecylamine, polyoxyethylene dodecylamine and polyoxyethylene octadecylamine.

Lastly, Miki is relied on as showing

that surfactants for measuring HDL, particularly nonionic surfactants such as polyoxyethylene oleyl ether, in addition to others, preferably those having HLB values of 12 to 17 are useful in reagent solutions which measure HDL cholesterol.

According to the Examiner then, it would have been obvious at the time the invention was made to modify Takayuki (measuring HDL-cholesterol using cholesterol esterase and cholesterol oxidase) based on the teachings of Hama (using nonionic surfactant), Miyauchi (the nonionic surfactant is oxyethylene dodecyllamine or octadecylamine) and Miki (using nonionic surfactant with a specified HLB value).

Previously, in order to reduce the issues, Applicants submitted a Declaration under Rule 132 of Yuki Katayama explaining that the method of the present invention was unexpectedly superior over the closest prior art by permitting accurate measurement of HDL cholesterol in a wide variety of sera samples. (Initially, Applicants wish to point out the Examiner has not questioned or disagreed with Applicants' showings of record, and the Examiner has not stated that Applicants' showings are not commensurate in scope with their claims. Nonetheless, solely in order to reduce the issues

and better expedite prosecution, Applicants have above amended their claims in even closer conformity with Yuki Katayama's Declaration.)

Instead, to the contrary, the Examiner states the pending claims are obvious because of what the prior art teaches. Put differently, as best understood the Examiner is apparently disregarding that the showings in Mr. Katayama's Declaration under Rule 132. That is, the Examiner circularly argues the Declaration is irrelevant because she has made out a *prima facie* case of obviousness. Of course, this is illogical because the Declaration would not be needed if there was no *prima facie* obviousness. And again, as noted above, the Examiner has neither questioned nor disagreed with Applicants' showings of record. For that reason alone, any *prima facie* case of obviousness has been rebutted on the record, and withdrawal thereof is respectfully requested.

The Examiner also states Applicants

argue that the instant method has specific sensitivity for a type of disease where other measurement methods do not work well, however the claims are not drawn to measurement of HDL cholesterol in sera samples from patients suffering from M. proteinemia. (Page 7, lines 17-19).

This is not well-understood. It is long-held the advantages of a process do not have to be recited in the claims since they are inherent to that process. Indeed, such advantages need not even be explicitly taught in the specification (and so, could not be claimed anyway). *In re Zenitz*, 333 F.2d 924 (CCPA 1964).

In any event, to complete the record, none of Takayuki or Hama mentions polyoxyethylene dodecylamine or polyoxyethylene octadecylamine. Only Miyauchi does, but Miyauchi teaches these surfactants (and others) can also be used for assaying

lipoproteins other than HDL. Thus, the operation of these surfactants is not taught in the prior art.

To the contrary, the present inventors have discovered that by using these specific nonionic surfactants together with albumin and a particular polyanion (dextran sulfate), measuring HDL cholesterol can be optimally attained. This combination is not suggested even in view of Miyauchi, which teaches that many combinations of surfactants and polyanions may be utilized.

However, none achieves the unexpected advantages shown in the Declaration under Rule 132 of record, which particularly evidences that Miyauchi's polyoxyethylene lauryl ether, polyoxyethylene cetyl ether and polyoxyethylene stearyl ether and polyoxyethylene oleyl ether all fail to achieve the unexpected advantages attained by the present invention.

In view of the above amendments and remarks, Applicants submit that all of the Examiner's concerns are now overcome and the claims are now in allowable condition. Accordingly, reconsideration and allowance of this application is earnestly solicited.

Claims 1-3, 38, 39, 41, 42 and 51 remain presented for continued prosecution.

Applicants' undersigned attorney may be reached in our New York office by telephone at (212) 218-2100. All correspondence should continue to be directed to our below listed address.

Respectfully submitted,

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